Delays in the Diagnosis and Treatment of Lung Cancer*

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Study objectives: This study was undertaken to measure delays of diagnosis and to assess the causes for those delays in patients with lung cancer. In addition, the relation of delay times and survival was analyzed.

Design: A retrospective study based on patient records. Dates for symptoms, visits to doctors, investigations, treatment, and death were recorded.

Setting: Patients who were found to have lung cancer at Turku University Hospital, Finland, during 2001.

Patients: Records of 132 patients were reexamined.

Results: The median delay in patient presentation from first symptoms to first appointment with a general practitioner (GP) was 14 days. The median delay by the GP before writing a referral was 16 days, the median referral delay was 8 days, the median delay from the first visit to a specialist until the diagnosis was 15 days, and the median treatment delay was also 15 days. Thirty percent of patients received treatment within 1 month from the first hospital visit, and 61% received treatment within 2 months. The median symptom-to-treatment delay was almost 4 months. The delay in seeing a specialist was shorter in patients with advanced cancer and small cell lung cancer. About half of our patients fulfilled the criteria of the British Thoracic Society recommendations. A longer specialist treatment delay seemed to correlate with better survival in advanced disease, but it was not an independent significant factor for survival.

Conclusions: Several reasons for long delays were found, but on many occasions patients underwent numerous consecutive procedures before a diagnosis of cancer was confirmed. Shortening the diagnostic and treatment delay times might be possible with little extra cost by a multidisciplinary team approach and by rapid access to carefully planned investigations, but decreasing the patient delay might be more difficult. This study shows that long specialist treatment delays are not correlated with worse prognosis in patients with advanced disease. In patients with more limited disease, the delay time may be more critical, and if curative treatment is the goal, the diagnostic process should proceed without needless delay to avoid a situation in which curable disease becomes incurable. (CHEST 2005; 128:2282–2288)

Key words: delay; diagnosis; lung cancer; survival; treatment; waiting time

Abbreviations: CI = confidence interval; GP = general practitioner; HR = hazard ratio; NSCLC = non-small cell lung cancer

Lung cancer is one of the most common and most lethal forms of cancer in several industrialized countries. In Finland, it was the second most common cancer in men (age-adjusted incidence rate per 100,000 population, 31.8) and the fourth most common in women (age-adjusted incidence rate per 100,000 population, 9.0) in 2001. Despite the presence of developed modalities for treatment, the prognosis for patients with lung cancer has remained poor, with the 5-year survival rate being approximately 10%. Unfortunately, most lung cancers are found too late for a cure; only about 20% of patients undergo a radical surgical procedure, which is the only curative treatment. Prevention is the primary goal in the fight against lung cancer, but nowadays lung cancer is also common in ex-smokers and nonsmokers, and we do not know how to prevent their cancer. Screening for lung cancer has not yet proved to decrease mortality, although early cancer
diagnosis has been associated with increased operability and a better prognosis. The factors that affect the prognosis in patients with lung cancer are stage, histology, performance status, comorbidity, age, and sex. Most of these factors are not modifiable. The stage is dependent on patient delays and on diagnostic workup both in general practice and in specialist units. Shortening the delay times might increase the number of patients with resectable tumors and, in that way, might improve survival.

The diagnostic delay from first symptoms to diagnosis in lung cancer patients has been determined to be approximately 3 months in earlier studies and has been estimated to be as long as 7 months in a Swedish study. Among others, the British Thoracic Society and the Joint Collegiate Council for Oncology have made recommendations on the times for referrals and waiting times in the treatment pathway. However, only a few studies have investigated the relation of delays and survival.

This study was undertaken to measure the delays of diagnosis, to assess the causes for delays in patients with lung cancer, to evaluate whether the lengths of the delays were acceptable according to the British recommendations, and to examine the relations between delays and survival.

**Materials and Methods**

The Finnish health-care system is based on public primary health care (general practitioners [GPs]) and on specialist health care in hospitals. Access to primary health care is easy, but in public health care a visit to a specialist is possible only by referral. The government covers the majority of the costs of health care. The district of Turku University Hospital consists of 58 municipalities that have their own health centers and a population of about 453,000 people. It is the only hospital with respiratory specialists and oncologists in the region. In Finland, diagnostic examinations for lung cancer are prioritized, and therapy is usually commenced without needless delay.

The records of all patients who were found to have lung cancer in 2001 at Turku University Hospital were reexamined retrospectively. Dates for symptoms, visits to doctors, investigations, treatment, and death were recorded. The dates of and reason for death were received from Statistics, Finland. Clinical staging according to the new international system was carried out, and the histologic type of cancer was recorded. The delays were classified as follows. The patient’s delay is the time from the first symptoms until the first visit to a doctor, who was in general, a GP. The delays of the doctors were divided into GP delay, which is the time from the date the patient visited the first doctor until the date the consultation request for a specialist was written. The referral delay is the time between the writing of the referral and the first appointment with the specialist. The specialist’s delay is the time from the first appointment until the diagnosis was made. The treatment delay is the time from the diagnosis until the treatment began.

The differences in the diagnostic delay in different histologies were analyzed with the Kruskal-Wallis test, and the correlation between the diagnostic delay and stage was analyzed with the Spearman correlation coefficient. Analyses to identify factors related to event times (delays and deaths) were based on the log-rank test and the Cox proportional hazards model. A p value of < 0.05 was considered to be significant. Statistical analyses were carried out using a statistical software package (SAS, version 8.2; SAS Institute; Cary, NC).

**Results**

Altogether, 133 new lung cancers were found. One patient record was not found, so 132 patients were included in this study. Of these, 95 patients (72%) were men, and the mean age of all patients was 69 years (Table 1). In total, 44 of the lung cancers (33%) were in the operable stage, and 25 patients (19%) of all patients; 23% of patients with non-small cell lung cancer (NSCLC) were operated on. The main reason for inoperability after the cancer was in the advanced stage was poor lung function. Among the patients who underwent surgery, one patient underwent explorative thoracotomy and five patients had local disease that was too advanced for radical resection (stage IIIB disease, four patients; stage IV disease, one patient). The definite diagnosis of 15 patients was not made before they underwent thoracotomy.

The median and mean delays are presented in Figure 1. The median patient’s delay was 14 days, the median referral delay was 8 days, and the median specialist’s delay was 15 days. The median treatment delay was calculated in patients who received forms of treatment other than the best supportive care (111 patients), and it was 15 days. In those patients who underwent surgery, the median delay from the first specialist

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>37 (28)</td>
<td>95 (72)</td>
</tr>
<tr>
<td>Age, yr</td>
<td>69 (46–85)</td>
<td>69 (50–88)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers and ex-smokers</td>
<td>25 (67)</td>
<td>92 (97)</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>12 (32)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell</td>
<td>9 (24)</td>
<td>40 (42)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>14 (38)</td>
<td>28 (29)</td>
</tr>
<tr>
<td>Small cell cancer</td>
<td>9 (24)</td>
<td>16 (17)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (14)</td>
<td>11 (12)</td>
</tr>
<tr>
<td>Disease stage†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-IIIA</td>
<td>44 (33)</td>
<td></td>
</tr>
<tr>
<td>IIIB-IV</td>
<td>85 (67)</td>
<td></td>
</tr>
<tr>
<td>Treatment†</td>
<td></td>
<td></td>
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<tr>
<td>Radical operation</td>
<td>19 (14)</td>
<td></td>
</tr>
<tr>
<td>Radiotherapy or chemotherapy</td>
<td>92 (70)</td>
<td></td>
</tr>
<tr>
<td>Supportive care</td>
<td>21 (16)</td>
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</tr>
</tbody>
</table>

*Values are given as No. (%) or mean (range).
†Values for men and women are combined.

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appointment until operation was 54 days. Twenty-two percent and 61% of patients, respectively, had undergone surgery within 4 and 8 weeks. The median delay from first symptoms to definite diagnosis was 98 days, and to treatment 112 days. The median delay between the first GP visit and diagnosis was 52 days, and between the first GP visit and the beginning of treatment 73 days. Two-thirds of the patients had received their diagnosis within 2 months and had received treatment within 3 months of the first visit to a GP (Fig 2). The median delay from first specialist appointment to treatment was 41 days. Thirty-eight percent of patients received treatment within 1 month and 75% received treatment within 2 months from the first specialist contact.

The median delay between the first specialist appointment and the final diagnosis was similar in men and women, it was similar in patients >70 years old and <70 years old, and it was not significantly different in patients who had undergone surgery. The median delay was shorter in patients with small cell lung cancer than in those with other histologic types of cancer (p = 0.0494). Also, in patients with advanced disease (ie, stages IIIb to IV), the delay was shorter than in those with limited disease (ie, stages I to IIIa) [median delay time, 13 vs 22 days, respectively; p = 0.0012], and among different delay times especially the referral delay and specialist’s delay were shorter than in those patients with limited disease.

The specific reasons for long delays were examined in those 35 patients whose median specialist’s delay combined with the referral delay was >50 days. Some patients may have had several reasons for the long delay, but in this analysis only the most important was taken into consideration. Among them, 13 patients were operated on, of whom 8 did not have the diagnosis confirmed before the operation. In eight of the patients who underwent surgery, the main reason for the long delay was the waiting time for an operation (25 to 55 days). Three patients did not want invasive diagnostic examinations. Seven patients either had poor lung function or other severe diseases, or they were very old and invasive investigations were not possible. Five patients were at first thought to have a benign disease and only after follow-up was the presence of a malignant disease deemed possible. There were four patients who waited for CT scans or CT needle biopsy for 18 to 36 days, and six patients underwent several procedures before receiving a diagnosis. Two patients had clinically extensive malignant disease, and histologic confirmation was obtained only after beginning radiotherapy or chemotherapy.

The recommendations of the British Thoracic Society are that the GP should immediately refer patients with obvious clinical evidence of lung cancer to a respiratory physician, and that the patients should have an appointment with a specialist within 1 week. The results of the investigations should be available and communicated to the patient within 2 weeks. There should be a maximum of 8 weeks between the first consultation with a respiratory physician and thoracotomy, and not more than 4 weeks between the acceptance to a surgeon’s waiting list and undergoing the thoracotomy. In the present study, the GP delay (median time, 16 days) was not quite within the acceptable limits, and one third of the patients waited >30 days for a referral to a

**Figure 1.** The median and mean delays, and the number of observations in the diagnostic workup.

**Figure 2.** Percentage of patients with delays of <7, 30, and 60 days.
specialist. Forty-eight percent of our patients went to the first specialist appointment within 1 week after the referral was written, and 48% had received the diagnosis within 2 weeks of the first visit to a specialist. However, about one third of the patients waited > 1 month for a definite diagnosis after the first appointment with a specialist. Sixty-one percent of patients underwent surgery within 8 weeks of the first consultation with a respiratory physician, and the median waiting time for surgery in those patients who were confirmed to have cancer before diagnosis was 30 days.

The overall survival rate at 1 year was 31%, and the rate at 2 years was 20%. To investigate the relation between delays and survival, the delay time between the first visit to a specialist and the date of the beginning of treatment was used. Only those patients with active treatment were included. The patients were divided into the following two groups: patients with a delay longer than or equal to the median time; and patients with a delay shorter than the median time. Patients with a delay longer than the median time had a 40% lower risk of dying compared with the patients with a shorter delay (hazard ratio [HR], 0.60; 95% confidence interval [CI], 0.39 to 0.91; \( p = 0.020 \)) [Fig 3, Table 2]. The result was similar whether we used the delay time from the first symptoms to treatment or from the first visit to a GP until the beginning of treatment; patients with longer delays seemed to have a better prognosis. This controversial finding was studied in more detail by taking into account the stage of disease. The HR estimate for long delays vs short delays changed very little after adjustment for the disease stage (HR, 0.65; 95% CI, 0.42 to 1.01; \( p = 0.054 \)). There was no significant interaction between the disease stage and the delay. The prognostic difference between patients with long and short delays was seen in patients with advanced disease (ie, stage IIIb to IV) \( [p = 0.022; \text{HR}, 0.53; 95\% \text{ CI}, 0.31 \text{ to } 0.91] \) but not in those with limited disease (ie, stage I to IIIa) \( [p = 0.807; \text{HR}, 1.11; 95\% \text{ CI}, 0.48 \text{ to } 2.54] \) [Fig 4]. The estimate of risk for death was favorable for the longer delay both in patients with stage IIIb disease and stage IV disease (stage IIIb disease: HR, 0.58; 95% CI, 0.22 to 1.52; stage IV disease: HR, 0.60; 95% CI, 0.31 to 1.17), although due to the small number of subjects in these subgroups the difference was not significant. In the multivariate analysis (which in addition to delay and disease stage included age, treatment, and type of cancer), the effect of delay time on prognosis diminished and was no more significant, but the point estimate for the risk of dying was still 16% lower (HR, 0.84; 95% CI, 0.52 to 1.34) in the group of patients who experienced a long delay (Table 2). Thus, the length of delay was not an independent risk factor for death. The two independent significant predictors for survival were higher age (HR, 1.71; 95% CI, 1.09 to 2.70; \( p = 0.002 \)) and surgical intervention (HR, 0.19; 95% CI, 0.09 to 0.44; \( p = 0.0001 \)).

**Discussion**

Studies calculating the growth of lung tumors based on mathematical models suggest that it takes 10 to 15 years from the appearance of the first cancer cell to the possibility of detecting a NSCLC by conventional chest radiograph. This indicates that the growth of a tumor is slow, and it seems unlikely that the prognosis is changed by the delay time of diagnosis. The time observed for lung tumors to double their volume ranges from 4 to 56 weeks, with a median time of 17 weeks. With the faster growing tumors, a doubling of the bulk of the primary tumor may occur together with local and distant spread during the diagnostic process. The growth of tumors is exponential, which means that even if the history is long, the growth at the time of discovery is more rapid, and long delays probably are a negative factor for the patient’s prognosis. It has been recommended that no more than 6 to 8 weeks should elapse between the patient’s first presentation to the GP and the operation.

Early detection of lung cancer has shown better survival rates among people screened with a chest radiograph or CT scan, although it has not yet been shown to decrease mortality. This points out that when the diagnosis is made early and the disease is limited the prognosis might be better. At present,
when screening is not routine practice, efforts to improve lung cancer survival have to concentrate on increasing the number of patients with resectable tumors.

This study was retrospective, and therefore some dates were missing (23% of the patients were missing the date of first symptoms), and the data were often presented inexactly (15% of patients were missing the date of the first visit to a GP, four patients were missing the referral date, and two patients were missing the date of the first appointment with a specialist). Therefore, the median and mean delays in the beginning of the diagnostic process might not be as reliable as they are after the date of referral.

The median delay time of 112 days from the first symptoms to the commencement of treatment was similar to results from the United Kingdom, was shorter than the time in two Swedish studies, and was longer than the time in a Polish study. In one of the Swedish studies, a diagnosis of lung cancer took a mean time of 7 months, of which 1.5 months were due to the patient and 5.5 months due to the doctors. The mean figures were high, with some exceptionally long delays, but the investigators concluded that even the median values seem too high and should be shortened. We also included patients with small cell cancer and patients with advanced disease who received only symptomatic treatment and whose delays were shorter, and this might explain the difference with the Swedish studies.

In the study of Ringbaek and colleagues, the average time between the first appointment with a specialist and operation was 69 days. The average delay from diagnosis to surgery was 26 days. In another study, the mean time from presentation to operation was 109 days. This included an average of 1 month before referral to a respiratory specialist, who then spent 2 months investigating the patient. After referral to a surgeon, surgery took place within a mean interval of 24 days. In the present study, the mean delay time from the first specialist appointment to operation was 120 days, and the median time was 54 days. This means that, on average, an operable patient had an approximately 2-month longer delay than those in other studies.

About half of our patients fulfilled the criteria of the British Thoracic Society recommendations. Besides these, several other national recommendations on delay times in the diagnosis and treatment of lung
cancer exist. The recommendations of the Swedish Lung Cancer Study Group\textsuperscript{14} are that in 80\% of all patients diagnostic tests should be completed within 4 weeks from consultation with a specialist and that treatment should start within 2 weeks thereafter. Sixty-six percent of our patients fulfilled the diagnostic delay criteria, and 49\% of our patients fulfilled the treatment delay criteria. In Canadian recommendations,\textsuperscript{16} a maximum of 4 weeks should elapse between the first visit to a GP and diagnosis, and the waiting time for surgery should not exceed 2 weeks. Our delays were far from these recommendations; only 26\% fulfilled the 4-week limit.

The present study points out that a shorter specialist’s delay is related to more advanced disease stage and supports the findings of a recent study.\textsuperscript{14} Even if this finding contradicts those of some other studies,\textsuperscript{7,13,17,18} the result seems logical; in patients with advanced disease, the diagnosis is made faster than in those with limited disease, in whom several investigations are needed before a diagnosis is obtained. Our study indicates that a longer specialist treatment delay is not associated with a worse outcome in lung cancer patients with advanced disease. On the contrary, the prognosis was worse in patients with shorter delays. This was also shown in the study by Myrdal et al.\textsuperscript{14} One explanation for this unexpected finding might be that when the tumor is small the delay is long, but prognosis is better than that in patients with advanced disease. Therefore, we cannot exclude the possibility that the delays have an effect on prognosis if the calculation is only based on correlations of diagnostic delays and prognosis. In the multivariate analysis, the negative association between delay and survival was preserved even if the delay was not an independent predictor for survival. Although several studies\textsuperscript{5,13,15,19,20} have shown that long delays have no effect on prognosis in patients with NSCLC, it seems likely that delays of 4 months, which approximate to one tumor volume-doubling time for NSCLC, will ensure that some tumors become inoperable. Lung cancer advances in stage during the diagnostic process, and this might have a confounding effect on the relation of delay and survival. This is not possible to measure and therefore cannot be controlled for. Furthermore, a delay of 3 or 4 months cannot be acceptable from the point of view of the patient, whose life is disrupted by multiple investigations and waiting times.

Even if the present study was of relatively small size and retrospective, it gives an idea about the delays in the diagnosis of lung cancer and made us assess where we could be faster. The delay of patients was quite long in some cases, but it may be the one delay time that is the most difficult to shorten. The delay in primary health care was too long according to the recommendations of the British Thoracic Society. A new electronic referral system might shorten the referral delay from writing the referral to the first specialist’s appointment to a few days. At the specialist level, considerable diagnostic delays occurred if several invasive procedures were needed to establish the diagnosis and/or operability of the tumor. Improvements are probably possible without much extra cost with a multidisciplinary team approach including a surgeon and by rapid access to carefully planned investigations. This study showed that long specialist treatment delays were not associated with worse prognosis in patients with advanced disease. Although delays seemed not to correlate with survival in patients with more limited disease, rapid diagnostic investigations without long delays might increase the number of resectable tumors and thereby improve the prognosis of lung cancer patients.

References